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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/840,085	04/24/2001	Alanna Schepartz Shrader	YU-P01-021	2186

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EXAMINER	
ALLEN, MARIANNE P	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 10/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/840,085	SHRADER ET AL.	
	Examiner	Art Unit	
	Marianne P. Allen	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 12-27* is/are pending in the application.

4a) Of the above claim(s) *14-18 and 20-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,12,13,19 and 23-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-5 and 12-27* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 4/22/02
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 6-11 have been cancelled. Claims 14-18 and 20-22 have been withdrawn as being directed to the non-elected invention. Claims 24-27 have been newly introduced. Claims 1-5, 12-13, 19, and 23-27 are under consideration by the examiner.

Applicant has previously elected SEQ ID NO: 23 for examination. The record clearly indicates that this was not a species election. However, the examiner has expanded examination to include the related sequences SEQ ID NOS. 24-29 in view of newly introduced claims 26 and 27. No other sequences are under consideration and the claims have only been examined to the degree that they reflect SEQ ID NOS: 23-29.

Applicant is advised that withdrawn claim14 contains an error in that it now lacks a terminal period (".").

Applicant's arguments with respect to claims 1-5, 12-13, 19, and 23-27 have been considered but are moot in view of the new ground(s) of rejection.

Specification

The description of the figures on pages 5-6 fail to reference by SEQ ID NO. the sequences disclosed in the drawings. See at least figures 2-7. Should any of these sequences not be present in the sequence listing, applicant is reminded that all sequences disclosed in the specification must be in compliance with 37 CFR 1.821-1.825.

Claim Rejections - 35 USC § 112

Claims 19 and 24-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicant's response of 7/2/03 introduced the limitation "at least 65% identical" to parts (c) and (d) of claim 19. No basis was pointed to and none is apparent for this limitation.

Claims 24-27 have been newly introduced. Claims 24-25 recite wherein the avian pancreatic polypeptide binds to the Bcl-X_L or Bcl2 protein. No basis has been pointed to for these claims and none is apparent. While the resulting modified protein may have this property, the unsubstituted protein does not. Claims 26-27 recite "wherein the avian pancreatic polypeptide comprises..." No basis has been pointed to for these claims and none is apparent. While the resulting modified protein may have this property, the unsubstituted protein does not. Furthermore, the specification discloses only the scaffold aPP of SEQ ID NO: 6 with SEQ ID NOS: 23-29 grafted upon it. It does not disclose any other avian pancreatic polypeptides comprising these sequences or modified to produce these peptides.

Claims 1-5, 12-14, 19, and 23-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NOS: 23-29 does not reasonably provide enablement for avian pancreatic polypeptides with the stated substitutions and properties. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The only avian pancreatic polypeptide that is disclosed as being modified is the 36 amino acid aPP sequence of SEQ ID NO: 6 (see page 9 of the specification). According to the

disclosure, amino acids 74-92 of Bak (the Bak-BH3 binding domain) are aligned with aPP. Computational analysis is performed to determine expected interactions. The results of this computer model are used to produce a phage display library of chimeric peptides that are artificial (not naturally occurring) and expected to have particular properties. The library is assayed for these properties. (See specification pages 14-15.) Note that the peptides of SEQ ID NOS: 27, 28, and 29 do not bind Bcl. As such, claims 26 and 27 embrace clearly inoperative embodiments. In addition, the specification does not identify additional peptides that are expected to have the stated properties and does not identify any other avian pancreatic polypeptides that could be modified as stated to produce peptides with the properties required by the claims. The specification does not clearly disclose where within SEQ ID NO: 6 the sequences represented by SEQ ID NOS: 23-29 are present. Particularly with respect to claims 1-5, 12-13, and 23-25, the claims provide no base structure to modify. There is insufficient guidance in the specification with respect to other avian pancreatic polypeptides as to how to modify such a polypeptide to result in the properties recited in the claims. This is an invitation to experiment and would constitute undue experimentation in view of the lack of guidance and unpredictability in the art.

Claims 13 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 recites "wherein the interaction between the known protein and the Bcl2 protein is inhibited." This claim is confusing. What is causing the inhibition? If the claimed modified

avian polypeptide is supposed to be an inhibitor and inhibit this interaction the claim doesn't make this clear.

Claim 23 is confusing in its dependency on claim 12 as the "known protein" identified as Bcl-2 in claim 12 is now required to be Bak in claim 23.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 12-13, 23, 24, and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Chittenden et al. (U.S. Patent No. 5,656,725).

SEQ ID NO: 10 of Chittenden et al. is a fragment of the Bak protein that binds to Bcl-X_L. See at least abstract, claims, and columns 18-20. SEQ ID NO: 10 is encompassed by instant SEQ ID NO: 30, matches 9 of 15 amino acids of instant SEQ ID NO: 23, and matches 10 of 15 amino acids of instant SEQ ID NO: 24. These claims recite no specific base structure or sequence that is modified nor a particular structure or sequence that results. No particular avian pancreatic polypeptide is recited as the base structure to be modified and no particular SEQ ID NO. is recited identifying the resulting product. It is further noted that the sequences that result are all artificial, non-naturally occurring peptides and thus the recitation of species (avian) and tissue (pancreatic) are given no patentable weight with respect to the resulting product. These are in a sense process limitations for producing a product (take unspecified avian pancreatic

polypeptide and substitute). However, a claim to a product is examined as a product independent of how it is derived. As such, SEQ ID NO: 10 can be considered to meet the limitations of an avian pancreatic polypeptide modified by substitution. SEQ ID NO: 10 of Chittenden et al. has at least twelve residues not in common with amino acids 1-15 of the avian pancreatic polypeptide (aPP) of instant SEQ ID NO: 6 and meets the alpha helix domain, interaction site, and binding functions required by the claims 1-5, 12-13, and 23-25. Review of the record reflects that applicants appear to believe that all of the claims require inclusion of some portion of the aPP scaffold, SEQ ID NO: 6. This is not correct. Use of the phrase "avian pancreatic polypeptide modified by substitution" in the claims does not provide such a limitation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 12-13, and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zondlo et al. (J. Am. Chem. Soc., 121:6938-939, 1999) in view of Sattler et al. (Science, 275:983-986, 1997).

Zondlo et al. dislcoses designing miniature proteins using avian pancreatic polypeptide (aPP) as a scaffold. The reference states that this strategy may be a general approach to the design of small, folded proteins that recognize protein targets with high affinity and specificity. (See at least page 6938, left column.) The Bcl-2 family and Bak protein are not disclosed.

Sattler et al. discloses that amino acids 72-87 of the Bak BH3 region bound tightly to Bcl-X_L. These protein interactions are important in apoptosis. Other peptides from Bak were evaluated for binding efficiency. (See at least abstract and page 983, right column, and Table 1.)

It would have been obvious to use the peptides in Sattler et al. in the method disclosed by Zondlo et al. to result in small, folded proteins that recognized the protein targets Bak and Bcl-X_L higher affinity and specificity. One would have been motivated to do so as such peptides would have been of interest in the study of apoptosis.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is 571-272-0712. The examiner can normally be reached on Monday-Thursday, 5:30 am - 1:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marianne P. Allen
Primary Examiner
Art Unit 1647

10/6/05

mpa